THE UNIVERSITY OF WISCONSIN
COLLEGE OF AGRICULTURE

Madison 6

DEPARTMENT OF GENETICS

September 5, 1955

Dear Luca:

Your ms. (and the giant postcard) finally arrived while we were visiting Denver about 10 days ago. Curiously, we had previously reciprocated with another giant card, which I hope you will have received. You can ascribe this to the rarefied atmosphere rather than the vino.

Your draft is superb! Not to mention the excellence of the work itself, not least on the chloramphenicol, which I had not seen in detail before. Your judgment on place of publication will have to be final, but I suspect it is colored by a somewhat defensive attitude from seeing Sevag's symposium. Keep in mind who organized it— it is far from representative (I must admit I have not yet seen it, as I am waiting for the book to arrive at our library!). At any rate, we shall have our innings at polemics in our book, and I recommedd that our paper be somewhat more reserved.

I would still recommend a genetic journal, especially with the amount of analytical detail given, and if so it should surelybe GENETICS. If you still prefer a bacteriological journal, then why not JOURNAL OF BACTERIOLOGY, which is the most widely circulated by far! Anyhow, you have the next and decisive word on this.

As to the text, I would not think of shortening it. I have only some minor suggestions having to do with the introduction and discussion, principally in line with the second paragpaph above. Also, I thought that (1) should be cast in a form that would show more obviously the functional dependence of r_1 on t. This makes k more complex; you can, if you like, simply redefine your k^{-1}(relative growth rate) as k_r/k_s for the later tables, and distinguish it from my k_d. This would be easier than directly recalculating all the k_d's.

Let the present form is OK. What do you think?

The attached sheets also give some other minor suggestions. If you want this to go either to Genetics or J. Bact., let me know your opinions and I will do the chorework of getting the ms. into press. You'd better furnish a good figure 2, however.

Luca- before I forget, may I ask you again if you wish to comment on my earlier question, whether you would be available at all for a position in this country. I have good reason to believe that several excellent openings may develop in the general area of medical genetics (which I take to include microbial no less than human), and I am anxious to know whether there would be any likelihood at all of your interest, so as to justify the presentation of your name. There is the obvious impediment of distance, but this is not such a large expense compared to the whole sums involved in a major appointment.

Yours,

Joshua Lederberg

I assume you have carbon copies of your text (as I do here).

General remarks.
There are a few, very minor points of wording that I have not troubled to indicate. If you do send this back for publication in an American journal, I will tend to them. On the whole, the style is (as I may already have said) superb, and there is nothing to shorten.
My only appreciable suggestions for revision concern the title, intro. and discussion, as you can see from the enclosures.
To my mind, the proof of preadaptation is a secondary aspect of the paper; it is primarily a rather thorough exercise in population genetics. You may remember Dubos' remark that you quoted to me, that if you really believed it, you wouldn't be "proving" it over and over again. In any event, a title that suggested the nature of the method would be preferable to "new".

The terms "best" and "fertile" are used throughout. "Best" is all right, but should be defined by a parenthesis, say on. p. 5: "The 'best' culture (i.e., the one with highest ratio of resistant cells)...." Fertile is more confusing; why not simply "positive" (coupled with a similar defining parenthesis.)?

p. 7 "delay to selection"; substitue: In order to lessen this obstacle A, the following means of reducing t, the number of generations, were tried. Elsewhere, I hope it is clear that t means this, not hours.

If k_d is used instead of k, a few changes would have to be made in the text. Perhaps it is better to leave your derivation of (1); I may have more comment later.
p. 8 cf. Ceppellini 1954?
table 4. Cycle 3. E = 6.5?

p.10 end: of the postadaptation theory.
p. 11 I would transpose this part on Dean and H. to the discussion, as you will see.

tables 6 ff. For typographical purposes, it would be better to use boldface or underlining than an arrow. How about boldface for one arrow, boldface italics for your double arrow.

table 9. refers to table 6?

p. 16 Should you add a word on how resistance was characterized? — I see you refer to figure 2 at p. 19; how about stability?
table 10. Which culture in table 9 has a double arrow?

Let me withdraw my paragraph deriving (1). However, you have an expression in R_t in the denominator, which seems to me simpler in e^t. Is the following incorrect?

$$1/r_1 = [1/Er_o - 1]\, e^{t(1-k)} + 1 \quad \text{or, to a good approximation}$$

$$= [1/Er_o]e^{t(1-k)} + 1.$$ which has a few less fractional exponents.

Then $r_1 = r_o$, calling $1-r_o = 1$, when $E = e^{t(1-k)}$, which compares to the similar "obvious" result in my derivation.

The formula holds, of course, only for a 1-resistant inoculum. Where you have E= 5, you must have a few instances of 2-resistant inocula, but this hardly matters.
I wait to hear from you, and will start serious work on the book at the earliest possible moment.

J